DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region 3 4651d

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973)526-6005

WARNING LETTER

CERTIFIED MAIL-
RETURN RECEIPT REQUESTED

April 19, 2004

Mr. Jay Wadekar
President and CEO
Able Laboratories Inc.
5&6 Hollywood Ct.
South Plainfield, NJ 07080-4204

File # 04-NWJ-09

Dear Mr. Wadekar:

During the period of January 15, 2004 through February 4, 2004 Investigator Margaret Sands from the U.S. Food and Drug Administration (FDA) New Jersey District Office conducted an inspection of your drug manufacturing facility at the above referenced address to determine your firm's compliance with the Postmarketing Adverse Drug Experience (PADE) reporting requirements of Title 21, Code of Federal Regulations, Part 314.80, 314.98 and Section 505(k) of the Federal Food, Drug and Cosmetic Act (the Act).

Based on our review of the inspection report, we concluded that your firm violated Section 301(e) of the Act because it failed to comply with 21 CFR 314.80 and Section 505(k)(1) of the Act. Section 505(k)(1) requires an applicant to establish and maintain records, and report data relating to clinical experience and other data or information for drugs for which an approved application is in effect.

Deviations from 21 CFR 314.80 include the following;

1. **Failure to submit to FDA 27 adverse drug experience reports received by your firm, for drug applications owned by your firm, as required in 21 CFR 314.80(c). These reports include, but are not limited to, the following:**

COMPLAINT	DATE	PRODUCT	ANDA#	EVENT
C02C002	3/4/02	Lithium Caps	76-121	Trouble concentrating
C02C003	3/6/02	Lithium Caps	76-121	Irritable
C02T062	10/24/02	Lithium Caps	76-121	Chest pains, rash, difficulty breathing

C02T001	**1/4/02**	**Methylphenidate Tablets**	**40-404**	**Trouble functioning, sedation**
C02C007	**11/13/02**	**Phentermine Caps**	**40-403**	**Caused minor strokes, admitted to ER**
C03T014	**2/4/03**	**Carisoprodol**	**40-421**	**Diarrhea, headache**
C03C029	**4/8/03**	**Lithium Caps**	**76-121**	**Elevated blood levels**
C03T080	**11/22/03**	**Tramadol Tabs**	**75-963**	**Loss of taste**

These 27 adverse drug experiences (ADEs) reported to your firm between 1/4/02 and 1/16/04, were never reported to the FDA. One of these complaints was by a patient taking Phentermine (Complaint C02C007). The patient was taken to an emergency room for a possible "...left midbrain or pontine infarct." Furthermore, your Vice President of Quality/Regulatory Affairs, Mr. Shashi Shah, told our investigator that your firm had never submitted any ADE reports to FDA.

All 27 referenced ADEs that you failed to submit to the FDA are regulated under 21 CFR 314.80. In addition to the 15-day submission of serious and unexpected ADEs to the FDA, 21 CFR 314.80 also requires the periodic reporting of all serious and expected ADEs as well as all non-serious ADEs. These periodic reports are required to be submitted quarterly for the first 3 years after a new drug approval and annually there after. You also have no record of submitting periodic reports to the FDA.

2. **Failure to develop adequate written procedures for the surveillance, receipt, evaluation, and reporting of Postmarketing Adverse Drug Experiences to FDA, as required by 21 CFR 314.80.**

Your firm has not developed adequate written procedures for the surveillance, receipt, evaluation, and reporting of Postmarketing Adverse Drug Experiences to the FDA. Our review of your internal control documents demonstrates this fact by the following examples:

1) A review of 3 of your internal complaint procedures, "Title: CUSTOMER COMPLAINTS," with effective dates of February 5,1998, October 23, 2002 and February 5, 2003, all state that the purpose of this document is to ensure that all complaints "are promptly investigated and documented in compliance with CFR 211.198 and CFR 310.305." 21 CFR 310.305 applies exclusively to the reporting of adverse events for marketed prescription drugs for human use without approved new drug applications. Your documents fail to reference 21 CFR 314.80, which addresses the reporting of ADEs for marketed prescription drugs with approved applications. Your facility manufactures such prescription drug products.

2) In part 5.0 of your "CUSTOMER COMPLAINT" file, it states that "All files will be retained for a minimum of [redacted] after the expiration date or 1 year after the date that the complaint was received, whichever is longer." In 21 CFR 314.80 (i), Recordkeeping, it states, "The applicant shall maintain for a period of [redacted] records of all known adverse drug experiences known to the applicant, including raw data and any correspondence relating to adverse drug experiences."

We acknowledge receipt of both the 27 MedWatch reports you submitted to the Agency, on or about February 20, 2004 and a copy of your revised SOP for the "Handling of Adverse Event Complaints," dated February 19, 2004.

The MedWatch forms which you submitted were on FDA form 3500, which is for the voluntary reporting of ADEs by healthcare workers and consumers. As a drug manufacturer, you must be reporting all domestic ADEs on FDA MedWatch form 3500A. Reports of foreign adverse drug events may be either reported on a MedWatch form 3500A or a CIOMS form. In addition, you may use a computer generated FDA form 3500A or alternate format as specified by 314.80 (f) (3). When using form 3500A, in addition to having an identifiable patient, at a minimum this report must also include an outcome, the identifiable reporter of the ADE, as well as the suspect drug. It is also required that you list the date of the report (Box B4) and the date received by the manufacturer (Box G4). It is also necessary to conduct follow up investigations if relevant information is missing from the initial MedWatch report. All follow-up information must be included on a form 3500A, or the alternative forms cited above, and linked to the initial report by a common unique manufacturing report number.

We also have the following comments regarding the revised SOPs you have submitted. Your most recent submission dated February 19, 2004 references the reporting of ADEs under 21 CFR 314.80. This document however, makes references to SOP# QA-090, which still contains misinformation, such as the maintaining of ADE records for less then the required 10 years. It could be helpful to create one SOP document for the processing of ADEs for both your approved products (21 CFR 314.80) and drugs not subject to approvals (21 CFR 310.305).

Neither the above list of deviations nor the Form FDA 483, "Inspectional Observations," which was presented to and discussed with Mr. Jay Wadekar, President and CEO, at the conclusion of the inspection, is intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and its regulations. The FDA expects drug manufacturers to establish reasonable mechanisms to assure surveillance, receipt, evaluation and submission of all adverse drug experiences to the FDA within established timeframes as required under 21 CFR 314.80, 310.305 and 314.98.

The specific violations noted in this letter are serious and may be symptomatic of serious underlying problems. You are responsible for investigating and determining the causes of the violations identified above and preventing recurrence of similar violations.

You should take prompt action to correct these deficiencies. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions may include, but are not limited to, seizure of your products and/or injunction. Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts.

We request that you reply in writing within fifteen (15) working days of receipt of this letter. If corrective actions cannot be completed within 15 working days, please state the reason for the delay and the timeframe within which corrective actions will be completed.

Your reply should be addressed to the New Jersey District Office, Food and Drug Administration, 10 Waterview Blvd., Parsippany, New Jersey 07054, Attn: Joseph F. McGinnis R.Ph, Compliance Officer.

Sincerely,

Diana Amador-Toro for

Douglas I. Ellsworth
District Director
New Jersey District